MISC. FEE TRANSMITTAL

Patent fees are subject to annual revision.

TOTAL AMOUNT OF PAYMENT	$500

Complete if Known	
Application Number	09/815,242
Filing Date	March 21, 2001
First Named Inventor	Robert Haselbeck
Examiner Name	Gibbs, Terra C
Group Art Unit	1635
Attorney Docket Number	E1025Y

METHOD OF PAYMENT

☒ Deposit Account

Deposit Account Number 13-2755 Deposit Account Name Merck & Co., Inc.

The Director is authorized to:

☒ Charge fee(s) indicated below ☒ Credit any overpayments

☒ Charge any additional fee(s) or underpayments of fee(s) under 37 CFR 1.16 and 1.17

FEE CALCULATION

FEES
Large Entity

Fee Code	Fee ($)	Fee Description	Fee Paid
1051	130	Surcharge - late filing fee or oath	
1051	130	Non-English Specification	
1812	2,520	For filing a request for *ex parte* reexamination	
1402	500	Filing a brief in support of an appeal	500
1452	500	Petition to revive - unavoidable	
1453	1,500	Petition to revive - unintentional	
1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	Submission of Information Disclosure Statement	
1809	790	Filing a submission after final rejection (37 CFR 1.129(a))	
1810	790	For each additional invention to be examined (37 CFR 1.129(b))	
1840	130	Statutory Terminal Disclaimer under 37 CFR 1.321	
		Other fee (specify) _____	
		Other fee (specify) _____	

TOTAL $500

SUBMITTED BY				Complete (if applicable)	
Typed or Printed Name	Sheldon O. Heber			Reg. Number	38,179
Signature		Date	05/17/2006	Deposit Account User ID	

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Appellant: Haselbeck, R. *et al.*

Application Number: 09/815,242

Attorney Docket Number: E1025Y

Filing Date: March 21, 2001

Title of the Invention: IDENTIFICATION OF ESSENTIAL GENES IN PROKARYOTES

Examiner: Gibbs, Terra C.

Art Unit: 1635

APPEAL BRIEF

37 C.F.R. 1.8 Certificate of Mailing

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents P.O. Box 1450 Alexandria VA 22313-1450, on the date appearing below.

MERCK & CO., INC.

By _____ Date May 17, 2006

Sheldon Heber

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REAL PARTY IN INTEREST

The real party in interest is Merck & Co., Inc. The application was acquired from Elitra Pharmaceuticals, Inc.

RELATED APPEALS AND INTERFERENCES

There are no related appeals and interferences.

STATUS OF CLAIMS

Claims 12, 31, 45-69, 77-87, 89-96, 100, 101, 103 and 104 are pending and stand rejected. The rejection of all the pending claims is appealed.

STATUS OF AMENDMENTS

An amendment after final rejection was mailed January 13, 2006, canceling claims 10, 11, 18-20, 29, 30, 37, 39, 70-76, 88, 98, 99, and 105 without prejudice to future prosecution. The cancelled claims were previously withdrawn from prosecution. The advisory action mailed February 22, 2006 indicated that for the purposes of appeal the amendment would be entered.

SUMMARY OF CLAIMED SUBJECT MATTER

The pending claims are directed to a method for screening a candidate compound for the ability to reduce cellular proliferation using a sublethal level of antisense nucleic acid directed to an identified target gene product (referred to herein a "yphC"[1]). The importance of yphC in cellular proliferation and its presence in different organisms is illustrated by the present application.

Pursuant to a restriction requirement, applicants elected SEQ ID NO: 1463 as the antisense sequence complementary to the *yphC* gene, SEQ ID NO 12600 as the yphC polypeptide, and SEQ ID NO: 4228 as the *yph*C nucleic acid encoding the gene product. (Office Action mailed October 19, 2005, at page 2, fifth paragraph.)

The importance of yphC to cellular proliferation is illustrated in the present application in Examples 1-3 and Tables 1B and VIIA. Examples 1-3 describe identification of genes involved in cellular proliferation using different antisense nucleic acids. (The present application at pages 114-126.) Antisense nucleic acids found to inhibit cellular proliferation were further characterized and the genes targeted by the antisense nucleic acid were identified.

Table VIIA identifies genes determined to be involved in cellular proliferation for a particular organism, and the corresponding gene in other organisms. The identification of SEQ ID NO: 12600 and sequence identity of corresponding genes from different organisms is provided on page 204, Locus ID NO SAU100521. The corresponding gene in *E. faecalis* was separated identified as involved in cellular proliferation. (Table VIIA, at page 198, Locus ID EFA103174.)

Table 1B references different antisense sequences used to identify cellular proliferation genes. *S. aureus* yphC (SEQ ID NO: 12600) was identified using the different antisense sequences of SEQ ID NOs: 1390, 1463, 1845, 2782, and 3283. (The present application at pages 466, 468, 479, 504, and 517.) *E. faecalis* yphC (SEQ ID NO: 10689) was identified using SEQ ID NO: 521. (The present application at page 446.)

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[1] The application itself does not refer to "yphC". The identified gene product has been designated yphC in the art. The particular designation "yphC" is not important for present appeal.

Independent claims 12, 31 and 100 describe a sensitization assay involving the steps of (a) producing a sensitized cell; (b) contacting the sensitized with a compound; and (c) determining the degree to which the compound inhibits proliferation of the sensitized cell relative to a nonsensitized cell. The sensitized cell is produced using a sublethal level of an antisense nucleic acid complementary to a portion of a nucleic acid encoding a gene product.

Claims 12, 31, and 100 differ in the description of antisense nucleic acid used to produce a target cell in step (a). The antisense sequence is related to the targeted gene encoding the target gene product. Claim 12 indicates that the target gene product is a gene product whose activity or amount is reduced by antisense nucleic acid comprising SEQ ID NO: 1463. Claim 31 indicates that the targeted gene product is selected from the group consisting of a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid of SEQ ID NO: 1463 a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid of SEQ ID NO: 1463, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected of SEQ ID NO: 1463 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 1463 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid of SEQ ID NO: 1463. Claim 100 indicates that the antisense sequence is either SEQ ID NO: 521, 1390, 1463, 1845, 2782, or 3283.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

I. Claims 78-84 stand rejected under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the written description requirement

II. Claims 12, 31, 45-69, 77-87, 89-96, 100, 101, 103 and 104 stand rejected as allegedly obvious based on the judicially created doctrine of obviousness-type double patenting in light of U.S. Patent No. 6,720,139

ARGUMENT

I. Claims 78-84 Fully Comply with the 35 U.S.C. §112, First Paragraph, Written Description Requirement by Providing both Structural and Functional Descriptions Demonstrating Possession of the Claimed Invention

Claims 78-84 provide both structural and functional descriptions demonstrating that applicants were in possession of the claimed invention. Structural descriptions are provided by reference to a nucleic acid having at least 97% (claim 78), at least 95% (claim 79), at least 90% (claim 80), at least 85% (claim 81), at least 80% (claim 82), or at least 70% (claim 83), sequence identity to SEQ ID NO: 1463; or a nucleic acid having at least 70% identity to at least 100 consecutive nucleotides of SEQ ID NO: 1463 (claim 84). A further functional description is provided by reference to antisense.

To meet the written description requirement a specification must reasonable convey to the skilled artisan that applicants were in possession of the invention as of the filing date. *In re Alton,* 76 F.3d 1168, 1172, 37 USPQ2d 1578, 1581 (Fed. Cir. 1996). The written description requirement can be satisfied by:

> Show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . *i.e.,* complete or partial structure, other physical and/or chemical properties, *functional characteristics when coupled with a known or disclosed correlation between function and structure*, or some combination of such characteristics.

Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 964, 63 USPQ2D 1609, 1613 (Fed. Cir. 2002), citing to and discussing Patent Office written description guidelines provided in 66 Fed. Reg. 1099, 1106 (January 5, 2001).

The examiner argues that the specification does not support the breadth of any nucleic acid with any particular percent identity to SEQ ID NO: 1463. (Advisory Action mailed February 22, 2006, page 2, first paragraph.) The examiner also argues that the claims embrace a very large genus, where no working examples of any nucleic acids with any particular percent identify to SEQ ID NO: 1463 that carry out the functional properties required in the claims are provided. (*Id.*) The examiner further argues that functionality alone is recited in the pending claims. (*Id.*)

The application illustrates that ability of SEQ ID NO: 1463 to provide antisense activity, identifies SEQ ID NO: 12600 as the *S. aureus* gene targeted by SEQ ID NO: 1463, provides examples of using other antisense nucleic acids to target SEQ ID NO: 12600, and identifies the corresponding gene in other organisms. (See Summary of the Invention *Supra.*) The rejection ignores the teachings provided by the ability of different sequences to have antisense activity, ignores the structural limitations provided in the claims based on SEQ ID NO; 1463, and ignores the known correlation between complementary base pairing which is important for antisense activity.

Compliance with the written description requirement for each of claims 78-84 is separately argued taking into account the structural description provided in the respective claim. As the noted degree of similarity to SEQ ID NO: 1463 decreases, the functional provision of antisense activity has a greater effect on the suitable of nucleic acids within the structural description.

A. Reference in Claim 78 to an Antisense Nucleic Acid Having at Least 97% Sequence Identity to SEQ ID NO: 1463 Provides Sufficient Identifying Characteristics to Comply With the Written Description Requirement

Claim 78 further limits claim 31 by indicating that the antisense nucleic acid comprises a nucleic acid having at least 97% sequence identity to SEQ ID NO: 1463. Reference to at least 97% sequence identity provides a structural limitation for the nucleic acid.

The application illustrates the ability of SEQ ID NO: 1463 to provide antisense activity. The skilled artisan would generally expect other nucleic acids falling within the scope of the 97% sequence identity to SEQ ID NO: 1463 to have antisense activity. The specificity of complementarity binding between nucleic acid bases contributing to antisense activity is well known in the art. (*E.g.,* A-T, G-C base pair binding.)

The examiner generally refers to the claims covering a large genus and that an astronomical number of embodiments are covered by the functional properties recited in the claims. (Office action mailed October 19, 2005, page 5, third paragraph.) The rejection is improperly based on the scope of the claims without any apparent consideration to the number of

species having the noted structural characteristics that would be expected to have antisense activity.

The Patent Office bears the initial burden of presenting a *prima facie* case of unpatentability. *In re Oetiker* 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). Given the ability of SEQ ID NO: 1463 to provide antisense activity, the 97% sequence identity to SEQ ID NO: 1463 indicated in the claims, and known relationship of complementary base pairing contributing to antisense activity, merely referring to a large genus does not establish a *prima facie* case of unpatentability.

While the provided rejection is written description, the examiner also indicates it would take a great deal of experimentation to determine appropriate antisense sequences. (Office action mailed October 19, 2005, page 5, third paragraph.) Based on the present application, it would not take undue experimentation to find appropriate antisense sequences to support the claims. As noted above, important structural and functional descriptions are provided. The skilled artisan need only perform routine testing of sequences within such descriptions (e.g., sequence of 97% identity) to confirm whether or not a particular sequence has the desired antisense activity.

Determining what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art. *In re Wands,* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The test for undue experimentation in not merely quantitative. *Id.* A considerable amount of experimentation is permissible, if it is merely routine, or if the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *Id.*

B. Reference in Claim 79 to an Antisense Nucleic Acid Having at Least 95% Sequence Identity to SEQ ID NO: 1463 Provides Sufficient Identifying Characteristics to Comply With the Written Description Requirement

Claim 79 further limits claim 31 by indicating that the antisense nucleic acid comprises a nucleic acid having at least 95% sequence identity to SEQ ID NO: 1463. Reference to at least 95% sequence identity provides a structural limitation for the nucleic acid.

The examiner generally refers to the claims covering a large genus and that an astronomic number of embodiments are covered by the functional properties recited in the claims. (Office action mailed October 19, 2005, page 5, third paragraph.) The rejection is improperly based on the scope of the claims without any apparent consideration to the number of species having the noted structural characteristic that would or arguable would not have antisense activity.

The Patent Office bears the initial burden of presenting a *prima facie* case of unpatentability. *In re Oetiker* 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). Given the ability of SEQ ID NO: 1463 to provide antisense activity, the at least 95% sequence identity to SEQ ID NO: 1463 indicated in the claim, and known relationship of complementary base pairing contributing to antisense activity, merely referring to a large genus does not establish a *prima facie* case of unpatentability.

While the provided rejection is written description, the examiner also indicates it would take a great deal of experimentation to determine appropriate antisense sequences. (Office action mailed October 19, 2005, page 5, third paragraph.) Based on the present application, it would not take undue experimentation to find appropriate antisense sequences to support the claims. Important structural and functional descriptions are provided. The skilled artisan need only perform routine testing of sequences within such descriptions to confirm whether or not a particular sequence has the desired antisense activity.

C. Reference in Claim 80 to an Antisense Nucleic Acid Having at Least 90% Sequence Identity to SEQ ID NO: 1463 Provides Sufficient Identifying Characteristics to Comply With the Written Description Requirement

Claim 80 further limits claim 31 by indicating that the antisense nucleic acid comprises a nucleic acid having at least 90% sequence identity to SEQ ID NO: 1463. Reference to at least 90% sequence identity provides a structural limitation for the nucleic acid.

The examiner generally refers to the claims covering a large genus and that an astronomic number of embodiments are covered by the functional properties recited in the claims. (Office action mailed October 19, 2005, page 5, third paragraph.) The rejection is improperly based on the scope of the claims without any apparent consideration to the number of

species having the noted structural characteristic that would or arguable would not have antisense activity.

The Patent Office bears the initial burden of presenting a *prima facie* case of unpatentability. *In re Oetiker* 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). Given the ability of SEQ ID NO: 1463 to provide antisense activity, the at least 90% sequence identity to SEQ ID NO: 1463 indicated in the claim, and known relationship of complementary base pairing contributing to antisense activity, merely referring to a large genus does not establish a *prima facie* case of unpatentability.

While the provided rejection is written description, the examiner also indicates it would take a great deal of experimentation to determine appropriate antisense sequences. (Office action mailed October 19, 2005, page 5, third paragraph.) Based on the present application, it would not take undue experimentation to find appropriate antisense sequences to support the claims. Important structural and functional descriptions are provided. The skilled artisan need only perform routine testing of sequences within such descriptions to confirm whether or not a particular sequence has the desired antisense activity.

D. Reference in Claim 81 to an Antisense Nucleic Acid Having at Least 85% Sequence Identity to SEQ ID NO: 1463 Provides Sufficient Identifying Characteristics to Comply With the Written Description Requirement

Claim 81 further limits claim 31 by indicating that the antisense nucleic acid comprises a nucleic acid having at least 85% sequence identity to SEQ ID NO: 1463. Reference to at least 85% sequence identity provides a structural limitation for the nucleic acid.

The examiner generally refers to the claims covering a large genus and that an astronomic number of embodiments are covered by the functional properties recited in the claims. (Office action mailed October 19, 2005, page 5, third paragraph.) The rejection is improperly based on the scope of the claims without any apparent consideration to the number of species having the noted structural characteristic that would or arguable would not have antisense activity.

The Patent Office bears the initial burden of presenting a *prima facie* case of unpatentability. *In re Oetiker* 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992).

Given the ability of SEQ ID NO: 1463 to provide antisense activity, the at least 85% sequence identity to SEQ ID NO: 1463 indicated in the claim, and known relationship of complementary base pairing contributing to antisense activity, merely referring to a large genus does not establish a *prima facie* case of unpatentability.

While the provided rejection is written description, the examiner also indicates it would take a great deal of experimentation to determine appropriate antisense sequences. (Office action mailed October 19, 2005, page 5, third paragraph.) Based on the present application, it would not take undue experimentation to find appropriate antisense sequences to support the claims. Important structural and functional descriptions are provided. The skilled artisan need only perform routine testing of sequences within such descriptions to confirm whether or not a particular sequence has the desired antisense activity

E. Reference in Claim 82 to an Antisense Nucleic Acid Having at Least 80% Sequence Identity to SEQ ID NO: 1463 Provides Sufficient Identifying Characteristics to Comply With the Written Description Requirement

Claim 82 further limits claim 31 by indicating that the antisense nucleic acid comprises a nucleic acid having at least 80% sequence identity to SEQ ID NO: 1463. Reference to at least 80% sequence identity provides a structural limitation for the nucleic acid.

The examiner generally refers to the claims covering a large genus and that an astronomic number of embodiments are covered by the functional properties recited in the claims. (Office action mailed October 19, 2005, page 5, third paragraph.) The rejection is improperly based on the scope of the claims without any apparent consideration to the number of species having the noted structural characteristic that would or arguable would not have antisense activity.

The Patent Office bears the initial burden of presenting a *prima facie* case of unpatentability. *In re Oetiker* 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). Given the ability of SEQ ID NO: 1463 to provide antisense activity, the at least 80% sequence identity to SEQ ID NO: 1463 indicated in the claim, and known relationship of complementary base pairing contributing to antisense activity, merely referring to a large genus does not establish a *prima facie* case of unpatentability.

While the provided rejection is written description, the examiner also indicates it would take a great deal of experimentation to determine appropriate antisense sequences. (Office action mailed October 19, 2005, page 5, third paragraph.) Based on the present application, it would not take undue experimentation to find appropriate antisense sequences to support the claims. Important structural and functional descriptions are provided. The skilled artisan need only perform routine testing of sequences within such descriptions to confirm whether or not a particular sequence has the desired antisense activity.

F. Reference in Claim 83 to an Antisense Nucleic Acid Having at Least 70% Sequence Identity to SEQ ID NO: 1463 Provides Sufficient Identifying Characteristics to Comply With the Written Description Requirement

Claim 83 further limits claim 31 by indicating that the antisense nucleic acid comprises a nucleic acid having at least 70% sequence identity to SEQ ID NO: 1463. Reference to at least 70% sequence identity provides a structural limitation for the nucleic acid.

The examiner generally refers to the claims covering a large genus and that an astronomic number of embodiments are covered by the functional properties recited in the claims. (Office action mailed October 19, 2005, page 5, third paragraph.) The rejection is improperly based on the scope of the claims without any apparent consideration to the number of species having the noted structural characteristic that would or arguable would not have antisense activity.

The Patent Office bears the initial burden of presenting a *prima facie* case of unpatentability. *In re Oetiker* 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). Given the ability of SEQ ID NO: 1463 to provide antisense activity, the at least 70% sequence identity to SEQ ID NO: 1463 indicated in the claim, and known relationship of complementary base pairing contributing to antisense activity, merely referring to a large genus does not establish a *prima facie* case of unpatentability.

While the provided rejection is written description, the examiner also indicates it would take a great deal of experimentation to determine appropriate antisense sequences. (Office action mailed October 19, 2005, page 5, third paragraph.) Based on the present application, it would not take undue experimentation to find appropriate antisense sequences to support the

claims. Important structural and functional descriptions are provided. The skilled artisan need only perform routine testing of sequences within such descriptions to confirm whether or not a particular sequence has the desired antisense activity.

G. Reference in Claim 84 to an Antisense Nucleic Acid Having at Least 70% Sequence Identity to a Nucleotide Sequence Comprising at Least 100 Consecutive Nucleotides of SEQ ID NO: 1463 Provides Sufficient Identifying Characteristics to Comply With the Written Description Requirement

Claim 84 further limits claim 31 by indicating that the antisense nucleic acid comprises a nucleic acid having at least 70% sequence identity to a nucleotide sequence comprising at least 100 consecutive nucleotides of SEQ ID NO: 1463. Reference to at least 70% sequence identity to a nucleotide sequence comprising at least 100 consecutive nucleotides of SEQ ID NO: 1463 provides a structural limitation for the nucleic acid.

The examiner generally refers to the claims covering a large genus and that an astronomic number of embodiments are covered by the functional properties recited in the claims. (Office action mailed October 19, 2005, page 5, third paragraph.) The rejection is improperly based on the scope of the claims without any apparent consideration to the number of species having the noted structural characteristic that would or arguable would not have antisense activity.

The Patent Office bears the initial burden of presenting a *prima facie* case of unpatentability. *In re Oetiker* 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). Given the ability of SEQ ID NO: 1463 to provide antisense activity, reference to at least 70% sequence identity to a nucleotide sequence comprising at least 100 consecutive nucleotides of SEQ ID NO: 1463 indicated in the claim, and known relationship of complementary base pairing contributing to antisense activity, merely referring to a large genus does not establish a *prima facie* case.

While the provided rejection is written description, the examiner also indicates it would take a great deal of experimentation to determine appropriate antisense sequences. (Office action mailed October 19, 2005, page 5, third paragraph.) Based on the present application, it would not take undue experimentation to find appropriate antisense sequences to support the claims. Important structural and functional descriptions are provided. The skilled artisan need

only perform routine testing of sequences within such descriptions to confirm whether or not a particular sequence has the desired antisense activity.

II. U.S. Patent No. 6,720,139 does not Render Claims 12, 31, 45-69, 77-87, 89-96, 100, 101, 103 and 104 Obvious Under the Judicially Created Doctrine of Obviousness-Type Double Patenting

U.S. Patent No. 6,720,139 (the '139 patent) includes claims directed to screening a candidate compound for the ability to reduce cellular proliferation using antisense nucleic acid. The examiner argues that since the species of the present application anticipates the genus of the claims granted in the '139 patent, the skilled artisan would conclude the invention provided in the pending claims are an obvious variation of the claims granted in the '139 patent. (Advisory Action mailed February 22, 2006, page 2, second paragraph.)

The pending claims distinguish the claims granted in the '139 patent, for example, by descriptions of particular sequences used the method. While the presence of a species anticipates a genus, a genus does not *pre se* anticipate or make obvious a species covered by the genus. Domination by itself does not give rise to double patenting. *In re Kaplan,* 789 F.2d 1574, 1577, 229 USPQ 678, 681 (Fed. Cir. 1986). In addition, "[t]he fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render the claimed compound obvious." *In re Baird,* 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994), citing to *In re Jones* 958 F.2d 347, 350, 21 USPQ2d 1941, 1943 (Fed. Cir. 1992).

An obviousness-type double patenting analysis generally involves: (1) determining the differences between the claims in the earlier patent and the claims in the later patent; and (2) determining whether the differences renders the claims patentable distinct. *Eli Lilly and Co. v. Barr Laboratories Inc.,* 251 F.3d 955, 968, 58 USPQ2d 1869, 1878 (Fed. Cir. 2001).

The pending claims differ from the claims granted in the '139 patent by providing descriptions of sequences. The rejection fails to indicate where the claims provided in the '139 specially provide such sequences.

Based on the different structural descriptions for sequences provided in the claims, different groups of claims are argued together as follows: (A) claims 12, 85-87 and 89-96; (B)

claims 31, 45-57, 101; (C) claims 58 and 59; (D) claims 60-67; (E) claim 68; (F) claim 69; (G) claim 77; (H) claims 78 and 79; (I) claims 80-84; and (J) claims 100, 103 and 104.

A. Claims 12 and 85-87 and 89-96

Claim 12 in step (a) provides a structural description. (See Claim Appendix, *infra.*) Claims 85-87 and 89-96 ultimately depend from claim 12. The obviousness-type double patenting rejection fails to take into account the structural description provided in step (a).

The rejection is based on the argument that the claims granted in the '139 patent cover the species provided in the rejected claims. As noted in Argument II *supra,* a genus does not *pre se* anticipate or make obvious a species covered by the genus.

B. Claims 31, 45-57, and 101

Claim 31 in step (a) provides a structural description. (See Claim Appendix, *infra.*) Claims 45-57 and 100 relate back to claim 31. The obviousness-type double patenting rejection fails to take into account the structural description provided in step (a).

The rejection is based on the argument that the claims granted in the '139 patent cover the species provided in the rejected claims. As noted in Argument II *supra,* a genus does not *pre se* anticipate or make obvious a species covered by the genus.

C. Claims 58 and 59

Claim 58 refers to:

> . . . wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 99% amino acid identity as determined using FASTA version 3.0t78 to SEQ ID NO: 12600 and a polypeptide whose activity may be complemented by a polypeptide of SEQ ID NO: 12600.

Claim 59 is long the same lines as claim 58, but indicates at least "95%" sequence identity. The obviousness-type double patenting rejection fails to take into account the provided structural descriptions.

The rejection is based on the argument that the claims granted in the '139 patent cover the species provided in the rejected claims. As noted in Argument II *supra,* a genus does not *pre se* anticipate or make obvious a species covered by the genus.

D. Claims 60-67

Claims 60-67 are along the same lines as claim 58, but indicate lower degrees of sequence similarity. The obviousness-type double patenting rejection fails to take into account the provided structural descriptions.

The rejection is based on the argument that the claims granted in the '139 patent cover the species provided in the rejected claims. As noted in Argument II *supra,* a genus does not *pre se* anticipate or make obvious a species covered by the genus.

E. Claim 68

Claim 68 refers to the polypeptide of 12600. The obviousness-type double patenting rejection fails to take into account the provided structural descriptions. The rejection is based on the argument that the claims granted in the '139 patent cover the species provided in the rejected claims. As noted in Argument II *supra,* a genus does not *pre se* anticipate or make obvious a species covered by the genus.

F. Claim 69

Claim 69 refers to:

> wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 34% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide having SEQ ID NO: 12600, a polypeptide having at least 39% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide having SEQ ID NO: 12600, a polypeptide having at least 42% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide having SEQ ID NO: 12600 and a polypeptide having at least 43% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide having SEQ ID NO: 12600.

The obviousness-type double patenting rejection fails to take into account the provided structural description.

The rejection is based on the argument that the claims granted in the '139 patent cover the species provided in the rejected claims. As noted in Argument II *supra,* a genus does not *pre se* anticipate or make obvious a species covered by the genus.

G. Claim 77

Claim 77 indicates the nucleic acid encoding the gene product is selected from the group consisting of: SEQ ID NOs: 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605. The obviousness-type double patenting rejection fails to take into account the provided structural description.

The rejection is based on the argument that the claims granted in the '139 patent cover the species provided in the rejected claims. As noted in Argument II *supra,* a genus does not *pre se* anticipate or make obvious a species covered by the genus.

H. Claims 78 and 79

Claims 78 and 79 indicate the antisense nucleic acid comprises a nucleic acid sequence with at least 97% or 95% sequence identity to SEQ ID NO: 1463. The obviousness-type double patenting rejection fails to take into account the provided structural description.

The rejection is based on the argument that the claims granted in the '139 patent cover the species provided in the rejected claims. As noted in Argument II *supra,* a genus does not *pre se* anticipate or make obvious a species covered by the genus.

I. Claims 80-84

Claims 80-84 indicate the antisense nucleic acid comprises a nucleic acid sequence with varying degrees of sequence identity to SEQ ID NO: 1463. At least 90% (claim 80), at least 85% (claim 81), at least 80% (claim 82), or at least 70% (claim 83), sequence identity to SEQ ID NO: 1463; or a nucleic acid having at least 70% identity to at least 100 consecutive nucleotides of SEQ ID NO: 1463 (claim 84). The obviousness-type double patenting rejection fails to take into account the provided structural description.

The rejection is based on the argument that the claims granted in the '139 patent cover the species provided in the rejected claims. As noted in Argument II *supra,* a genus does not *pre se* anticipate or make obvious a species covered by the genus.

J. Claims 100, 103 and 104

Claim 100 refers to an antisense nucleic acid selected from the group consisting of SEQ ID NOs: 521, 1390, 1463, 1845, 2782 and 328. Claims 103 and 104 relate back to claim 100. The obviousness-type double patenting rejection fails to take into account the provided structural description.

The rejection is based on the argument that the claims granted in the '139 patent cover the species provided in the rejected claims. As noted in Argument II *supra,* a genus does not *pre se* anticipate or make obvious a species covered by the genus.

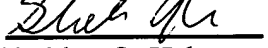
CONCLUSION

Appellant request that the Board of Patent Appeals and Interferences reverse the outstanding rejections of claims 12, 31, 45-69, 77-87, 89-96, 100, 101, 103 and 104.

Appellants note that the advisory action refers to claims 77, 87, 100 and 104 containing sequences withdrawn from prosecution. (Advisory Action mailed February 22, 2006, page 2, first paragraph.) Claim 77, 87, 100 and 104 also contain subject matter covering the elected species and, thus, the claims were not withdrawn from prosecution. No rejection based on the presence of the different sequences was provided. Restriction practice under § 121 does not provide a basis for rejecting a particular claim. *In re Weber, Soder and Boksay,* 580 F.2d 455, 458-459, 198 USPQ 328 (CCPA 1978).

Please charge deposit account 13-2755 for fees due in connection with this appeal brief. If any time extensions are needed for the timely filing of the present appeal brief, appellant petition for such extensions and authorize the charging of deposit account 13-2755 for the appropriate fees.

Respectfully submitted,

By 

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CLAIMS APPENDIX

12. A method for screening a candidate compound for the ability to reduce cellular proliferation comprising the steps of:

(a) providing a sublethal level of an antisense nucleic acid complementary to at least a portion of a nucleic acid encoding a gene product in a cell to reduce the activity or amount of said gene product in said cell, thereby producing a sensitized cell, wherein said gene product is a gene product whose activity or amount is reduced by an antisense nucleic acid comprising a nucleotide sequence of SEQ ID NO: 1463, provided that cell is a prokaryotic organism;

(b) contacting said sensitized cell with a compound; and

(c) determining the degree to which said compound inhibits proliferation of said sensitized cell relative to a nonsensitized cell.

31. A method for screening a candidate compound for the ability to reduce cellular proliferation comprising:

(a) providing a sublethal level of an antisense nucleic acid complementary to at least a portion of a nucleic acid encoding a gene product in a cell to reduce the activity or amount of said gene product in said cell, thereby producing a sensitized cell, wherein said gene product is selected from the group consisting of a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid of SEQ ID NO: 1463 a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid of SEQ ID NO: 1463, a gene

product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected of SEQ ID NO: 1463 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 1463 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid of SEQ ID NO: 1463; provided that said cell is a prokaryotic organism;

(b) contacting said sensitized cell with a compound; and

(c) determining the degree to which said compound inhibits the growth of said sensitized cell relative to a nonsensitized cell.

45. The method of Claim 31, wherein determining the degree to which said compound inhibits proliferation of said sensitized cell relative to a nonsensitized cell comprises determining whether said compound inhibits the growth of said sensitized cell to a greater extent than said compound inhibits the growth of said nonsensitized cell.

46. The method of Claim 31, wherein said gene product is from an organism other than *E. coli*.

47. The method of Claim 31, wherein said cell is an organism other than *E. coli*.

48. The method of Claim 31, wherein said sensitized cell is a pathogenic microorganism.

49. The method of Claim 31, wherein said sensitized cell is a Gram positive bacterium.

50. The method of Claim 49, wherein said Gram positive bacterium is selected from the group consisting of *Staphylococcus* species, *Streptococcus* species, *Enterococcus* species, *Mycobacterium* species, *Clostridium* species, and *Bacillus* species.

51. The method of Claim 50, wherein said bacterium is *Staphylococcus aureus*.

52. The method of Claim 50, wherein said *Staphylococcus* species is coagulase negative.

53. The method of Claim 51, wherein said bacterium is selected from the group consisting of *Staphylococcus aureus* RN450 and *Staphylococcus aureus* RN4220.

54. The method of Claim 31, wherein said antisense nucleic acid is transcribed from an inducible promoter.

55. The method of Claim 31, further comprising the step of contacting said cell with a concentration of inducer which induces transcription of said antisense nucleic acid to a sublethal level.

56. The method of Claim 31, wherein growth inhibition is measured by monitoring optical density of a culture medium.

57. The method of Claim 31, wherein said gene product is a polypeptide.

58. The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 99% amino acid identity as determined using FASTA version 3.0t78 to SEQ ID NO: 12600 and a polypeptide whose activity may be complemented by a polypeptide of SEQ ID NO: 12600.

59. The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 95% amino acid identity as determined using FASTA version 3.0t78 to SEQ ID NO: 12600 and a polypeptide whose activity may be complemented by a polypeptide of SEQ ID NO: 12600.

60. The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 90% amino acid identity as determined using FASTA version 3.0t78 to SEQ ID NO: 12600 and a polypeptide whose activity may be complemented by a polypeptide of SEQ ID NO: 12600.

61. The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 85% amino acid identity as determined using FASTA version 3.0t78 to SEQ ID NO: 12600 and a polypeptide whose activity may be complemented by a polypeptide of SEQ ID NO: 12600.

62. The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 80% amino acid identity as

determined using FASTA version 3.0t78 to SEQ ID NO: 12600 and a polypeptide whose activity may be complemented by a polypeptide of SEQ ID NO: 12600.

63. The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 70% amino acid identity as determined using FASTA version 3.0t78 to SEQ ID NO: 12600 and a polypeptide whose activity may be complemented by a polypeptide of SEQ ID NO: 12600.

64. The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 60% amino acid identity as determined using FASTA version 3.0t78 to SEQ ID NO: 12600 and a polypeptide whose activity may be complemented by a polypeptide of SEQ ID NO: 12600.

65. The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 50% amino acid identity as determined using FASTA version 3.0t78 to SEQ ID NO: 12600 and a polypeptide whose activity may be complemented by a polypeptide of SEQ ID NO: 12600.

66. The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 40% amino acid identity as determined using FASTA version 3.0t78 SEQ ID NO: 12600 and a polypeptide whose activity may be complemented by a polypeptide of SEQ ID NO: 12600.

67. The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to SEQ ID NO: 12600 and a polypeptide whose activity may be complemented by a polypeptide of SEQ ID NO: 12600.

68. The method of Claim 57, wherein said polypeptide is 12600.

69. The method of Claim 57, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 34% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide having SEQ ID NO: 12600, a polypeptide having at least 39% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide having SEQ ID NO: 12600, a polypeptide having at least 42% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide having SEQ ID NO: 12600 and a polypeptide having at least 43% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide having SEQ ID NO: 12600.

77. The method of Claim 31, wherein said nucleic acid encoding said gene product is selected from the group consisting of SEQ ID NOs: 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605.

78. The method of Claim 31, wherein said antisense nucleic acid comprises a nucleic acid having at least 97% nucleotide sequence identity to SEQ ID NO: 1463.

79. The method of Claim 31, wherein said antisense nucleic acid comprises a nucleic acid having at least 95% nucleotide sequence identity to SEQ ID NO: 1463.

80. The method of Claim 31, wherein said antisense nucleic acid comprises a nucleic acid having at least 90% nucleotide sequence identity to SEQ ID NO: 1463.

81. The method of Claim 31, wherein said antisense nucleic acid comprises a nucleic acid having at least 85% nucleotide sequence identity to SEQ ID NO: 1463.

82. The method of Claim 31, wherein said antisense nucleic acid comprises a nucleic acid having at least 80% nucleotide sequence identity to SEQ ID NO: 1463.

83. The method of Claim 31, wherein said antisense nucleic acid comprises a nucleic acid having at least 70% nucleotide sequence identity to SEQ ID NO: 1463.

84. The method of Claim 31, wherein said antisense nucleic acid comprises a nucleic acid having at least 70% nucleotide sequence identity to a nucleotide sequence comprising at least 100 consecutive nucleotides of SEQ ID NO: 1463.

85. The method of Claim 12, wherein determining the degree to which said compound inhibits proliferation of said sensitized cell relative to a nonsensitized cell comprises determining whether said compound inhibits the growth of said sensitized cell to a greater extent than said compound inhibits the growth of said nonsensitized cell.

86. The method of Claim 12, wherein said prokaryotic organism is either *Staphylococcus aureus* or *Enteroccus faecalis*.

87. The method of Claim 86, wherein said prokaryotic organism is *Staphylococcus aureus* and said nucleotide sequence is selected from the group consisting of SEQ ID NOs: 1390, 1463, 1845, 2782 and 3283.

89. The method of Claim 12, wherein said sensitized cell is a Gram positive bacterium.

90. The method of Claim 89, wherein said Gram positive bacterium is selected from the group consisting of *Staphylococcus* species, *Streptococcus* species, *Enterococcus* species, *Mycobacterium* species, *Clostridium* species, and *Bacillus* species.

91. The method of Claim 90, wherein said bacterium is *Staphylococcus aureus*.

92. The method of Claim 90, wherein said *Staphylococcus* species is coagulase negative.

93. The method of Claim 91, wherein said bacterium is selected from the group consisting of *Staphylococcus aureus* RN450 and *Staphylococcus aureus* RN4220.

94. The method of Claim 12, wherein said antisense nucleic acid is transcribed from an inducible promoter.

95. The method of Claim 12, further comprising the step of contacting said cell with a concentration of inducer which induces transcription of said antisense nucleic acid to a sublethal level.

96. The method of Claim 12, wherein growth inhibition is measured by monitoring optical density of a culture medium.

100. A method for screening a candidate compound for the ability to reduce cellular proliferation comprising the steps of:

(a) providing a sublethal level of an antisense nucleic acid selected from the group consisting of SEQ ID NOs: 521, 1390, 1463, 1845, 2782 and 3283, wherein said antisense nucleic acid reduces the activity or amount of a gene product required for cellular proliferation, thereby producing a sensitized cell, provided that said sensitized cell is a prokaryotic organism;

(b) contacting said sensitized cell with a compound; and

(c) determining the degree to which said compound inhibits proliferation of said sensitized cell relative to a nonsensitized cell.

101. The method of Claim 48, wherein said pathogenic mircoorganism is selected from the group consisting of *Anaplasma marginale, Aspergillus fumigatus, Bacillus anthracis, Bacterioides fragilis Bordetella pertussis, Burkholderia cepacia, Campylobacter jejuni, Candida albicans, Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis, Candida parapsilosis, Candida guilliermondii, Candida krusei, Candida kefyr* (also called *Candida*

pseudotropicalis), *Candida dubliniensis, Chlamydia pneumoniae, Chlamydia trachomatus, Clostridium botulinum, Clostridium difficile, Clostridium perfringens, Coccidiodes immitis, Corynebacterium diptheriae, Cryptococcus neoformans, Enterobacter cloacae, Enterococcus faecalis, Enterococcus faecium, Escherichia coli, Haemophilus influenzae, Helicobacter pylori, Histoplasma capsulatum, Klebsiella pneumoniae, Listeria monocytogenes, Mycobacterium leprae, Mycobacterium tuberculosis, Neisseria gonorrhoeae, Neisseria meningitidis, Nocardia asteroides, Pasteurella haemolytica, Pasteurella multocida, Pneumocystis carinii, Proteus vulgaris, Pseudomonas aeruginosa, Salmonella bongori, Salmonella cholerasuis, Salmonella enterica, Salmonella paratyphi, Salmonella typhi, Salmonella typhimurium, Staphylococcus aureus, Listeria monocytogenes, Moxarella catarrhalis, Shigella boydii, Shigella dysenteriae, Shigella flexneri, Shigella sonnei, Staphylococcus epidermidis, Streptococcus pneumoniae, Streptococcus mutans, Treponema pallidum, Yersinia enterocolitica, Yersinia pestis* and any species falling within the genera of any of the above species.

103. The method of Claim 100, wherein said prokaryotic organism is either *Staphylococcus aureus* or *Enteroccus faecalis*.

104. The method of Claim 103, wherein said prokaryotic organism is *Staphylococcus aureus* and said antisense nucleic acid is selected from the group consisting of SEQ ID NOs: 1390, 1463, 1845, 2782 and 3283.

EVIDENCE APPENDIX

None

RELATED PROCEEDINGS APPENDIX

None